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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,300	TETZNER ET AL.	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to papers filed 12/14/2009.

2. Currently Claims 1-28 are pending. Claims 29-31 have been cancelled.

3. The following rejections are reiterated. Response to arguments follows.

4. This action is FINAL.

Withdrawn Rejections

5. The rejection of the claims under 35 USC 112/2nd paragraph made in section 4 of the previous office action is moot based upon amendments to the claims.

6. The obviousness type double patenting rejection made over application 10/482433 made in section 10 of the previous office action has been withdrawn based upon arguments to the claims. Specifically, the limitation in application 10/482433 requiring detecting the differences between the molecular weights of two individual strands.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-2 and 4-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eads et al. (Nucleic acids Research 2000 Vol. 28 p. e32) in view of Solinas et al. (Nucleic acids Research 2001 Vol. 29 p. e96).

Eads et al. teaches a method for detecting of cytosine methylation (abstract).

With regard to Claim 1 step a, Eads et al. teaches reacting the DNA from tissue samples with a chemical (e.g. sodium bisulfite) to change unmethylated cytosine to uracil (p. ii 1st column last full sentence). With regard to Claim 1 step b, Eads et al. teaches PCR amplification with a polymerase, at least one primer, and a probe (p ii 2nd column Methylight primer and probe sequences and Figure 1). However, Eads et al. does not teach that the primer is joined with a probe via a linker. With regard to Claim 1 step c-e, Eads et al. teaches separating the primer strand and detection whether or not hybridization of the probe has occurred (figure 1).

With regard to Claim 2, Eads et al. teaches reacting the DNA with sodium bisulfite (p. ii 1st column last full sentence).

With regard to Claims 4-5, Eads et al. teaches a method of MSP RT-PCR (p. ii 1st column last paragraph and 2nd column 1st paragraph).

With regard to Claim 6, Eads et al. teaches a probe that has two signal components that are proximity to one another (p. ii 2nd column 2nd paragraph).

With regard to Claim 7, Eads et al. teaches quencher-florescent dye pair (p. ii 2nd column 2nd paragraph).

With regard to Claim 17, Eads et al. teaches that several sequences are simultaneously amplified (p. ii 2nd column 2nd and 3rd paragraphs).

With regard to Claim 29, Eads et al teaches a method of using for diagnosing mismatching in genes associated with cancer disorders (abstract).

However, Eads et al. does not teach that the primer is joined with a probe via a linker.

Solinas et al. teaches using Scorpion primers in PCR assays (abstract). With regard to Claim 1, Solinas et al. teaches a primer whose 5' end is joined with a probe via a linker (e.g. Scorpion primer) (Figure 1).

With regard to Claim 8, Solinas et al. teaches the probe forms a hairpin shape (p. 1 2nd column 1st paragraph).

With regard to Claim 9, Solinas et al. teaches the probe bears two signal components separated in the inactive form and activated after hybridization (Figure 1A).

With regard to Claim 10, Solinas et al. teaches detecting the signal using FRET (p. 3 1st column 1st paragraph).

With regard to Claim 11, Solinas et al. teaches a duplex Scorpion format wherein there is a signal on the probe and a signal on another oligonucleotide (Figure 1B).

With regard to Claim 12, Solinas et al. teaches detecting the signal using FRET (p. 3 1st column 1st paragraph).

With regard to Claim 13, Solinas et al. teaches a duplex Scorpion format wherein there is a signal on the probe and a signal on another oligonucleotide thereby separating the signals in the inactive form (Figure 1B).

With regard to Claim 14, Solinas et al. teaches a method wherein the probe comprises a signal and the other oligonucleotide bears a signal and under hybridization there is a signal (Figure 1b).

With regard to Claim 15, Solinas et al. teaches detecting the signal using FRET (p. 3 1st column 1st paragraph).

With regard to Claim 16 Solinas et al. teaches another binder binds in immediate proximity to the probe (Figure 1B).

With regard to Claim 18, Solinas et al. teaches that two scorpion primers can be used (Table 2).

With regard to Claim 19, Solinas et al. teaches that each Scorpion primer has a different signal (Table 2).

With regard to Claims 20, 21, and 28, Solinas et al. teaches Scorpion primers can be used to detect differences in nucleic acid structure (abstract). It would be obvious to design Scorpion primers to detect methylation and nonmethylated areas of the nucleic acid to use the primers in the methylation assay of Eads et al. Eads et al. teaches designing probes which hybridize to methylated and nonmethylated nucleic acid structures (Figure 1 of Eads et al.).

With regard to Claims 22-24, Solinas et al. teaches a probe with a quencher and a dye molecule which are in the inactive form when in spatial proximity (e.g. hairpin

form) and are activated by hybridization of the probe to a primer extension product (Figure 1A).

With regard to Claims 25-27, Solinas et al teaches an assay wherein the probe comprises a dye molecular and another oligonucleotides comprises a quencher and when the two are close they are inactive but after hybridization they are active (e.g. a duplex) (Figure 1B).

Therefore it would have been prime facie obvious to one of ordinary skill in the art to modify the methylation method of Eads et al. to include Scorpion primers linked to probes as taught by Solinas et al. The ordinary artisan would be motivated to modify the methylation method of Eads et al. to include Scorpion primers linked to probes as taught by Solinas et al., because Solinas et al. teaches the use of Scorpion primers in PCR assays allows an intermolecular probe-target interaction which results in a very fast and reliable detection system (p. 1 2nd column 2nd paragraph). Therefore the ordinary artisan would be motivated to use Scorpion primers to detect methylation and nonmethylation sites fast and reliably.

Response to Arguments

The reply traverses the rejection. A summary of the arguments presented in the reply is provided below with a response to arguments following.

(A) The reply asserts that based upon the method of Eads et al. there would have been no reason to attempt to modify the MehtyLight method by including the Scorpion primers linked to probes as taught by Solinas et al. (p. 11 last paragraph).

The reply asserts that the method of Eads et al. is taught to have advantages of being highly specific, sensitive, and reproducible and being compatible with very small amounts of template DNA (p. 11 last paragraph pointing to page ii 1st column 2nd paragraph of Eads et al). The reply asserts that based upon reading the passage a person of ordinary skill in the art would not have been motivated to further develop methylation assays to arrive at some advantages mentioned by the instant application (p. 11 last paragraph). The reply asserts that the benefits of the Scorpion primers taught by Solinas are basically similar to those of the instant method and prove a fast and reliable detection system and gives a lower background than Taqman probes (p. 11 last paragraph).

The reply asserts that it would not be obvious to modify a method in order to arrive at the additional advantages of detecting the methylation status of short fragments as claimed by the instant application (p. 12 1st paragraph). The reply asserts that in the instant application that the motivation to modify the MethyLight assay by including the Scorpion primers was to optimize the MehtyLight for the methylation analysis of short fragments without decreasing the specificity of the assay (p. 12 1st paragraph). The reply asserts that without reading the cited references there was no incentive for the ordinary artisan to develop an assay with the same advantages as disclosed in both cited references (p. 12 1st paragraph). The reply asserts that the instant method claims the surprising effect of combining the MethyLight assay with the scorpion primers to arrive at detecting short sample DNA fragments (p. 12 1st paragraph). The reply asserts that the advantage of the scorpion method to be well

suited for analysis of short DNA fragments is an advantage that has only been realized by the instant applicants (p. 12 1st paragraph).

These arguments have been fully reviewed but have not been found persuasive.

The reply seems to be asserting that because MethyLight assay has the same advantages as scorpion method (e.g. highly specific, sensitive, and reproducible and being compatible with very small amounts of template DNA) the ordinary artisan would have no motivation to combine the two methods. This is not persuasive, because even if two methods have the same type of advantages, it would be obvious for the ordinary artisan to use scorpion primers in the method of Eads et al. to determine if the use of Scorpion primers increases the sensitivity of the Eads method. Solinas et al. teaches that the use of Scorpion primers in PCR assays (the Eads method is a type of PCR) allows for a fasters and more reliable detection system because of the intermolecular probe-target interactions (p. 1 2nd column 2nd paragraph). Further, it would be obvious to combine known prior method art elements (e.g. the scorpion primers of Solinas et al and the Methylight method of Eads et al) to arrive at a method that yield the predictable result of being a fast and reliable detection method.

(B) The reply asserts that if there existed only a finite number of identified predictable solutions to arrive at the above mentioned advantages that the invention could be argued to be obvious (p. 12 last paragraph). The reply asserts that the approach was not obvious since there are numerous possible choices of primers to be used in DNA methylation analysis (p. 13 1st paragraph). The reply asserts that Eads et al. does not

mention which of the parameters of their method are critical to arrive at the mentioned advantages and how alternative primers like Scorpion primers could effect or improve the method (p. 13 1st paragraph). The reply asserts that the person of ordinary skill in the art would not have had any motivation to choose the Scorpion primers from all of the possible primers in order to modify the MehtyLight assay (p. 13 1st paragraph).

These arguments have been fully reviewed and have not been found persuasive.

Solinas et al. teaches that these scorpion primers can be used in PCR assays to produce a fast and reliable detection system (p. 1 2nd column 2nd paragraph). Eads et al. teaches a method of performing a MSP RT-PCR assay (p. ii 1st column last paragraph and 2nd column 1st paragraph). The ordinary artisan would be motivated to choose primers which have been shown to work in PCR assays in a fast and reliable manner. Solinas et al. teaches such scorpion primers. It would be obvious to the ordinary artisan that use of such primers in a PCR assay (such as the one taught by Eads et al) would have the predictable result of detecting the methylation status in a sample. As such the art of time of filing suggests that Scorpion primers can be used in PCR assays and therefore the art suggests a reasonable expectation of success that such primers would be used in the assay of Eads et al and produce a fast and reliable detection system.

(C) The reply asserts that the methods of MethyLight and Scorpion primers were both known by 1999 (p. 13 last paragraph). The reply asserts that the instant application foreign priority claimed is not until 2003 (p. 13 last paragraph). The reply asserts that it

was over 4 years between the two, however, there is no prior art documents indicating that this method would be obvious (p. 14 1st paragraph).

These arguments have been fully reviewed but have not been found persuasive.

Although the art does not provide a method of MethyLight using Scorpion primers, based upon the teaching of methylight (Eads et al.) and Scorpion primers (Solinas et al) it would have been prima facie obvious to combine the two known molecular methods. The reply has not brought in any evidence that the combination of these two methods would have been unpredictable to the ordinary artisan at the time of filing. The reply that no one has ever combine the two methods is insufficient to show that such a combination would be unpredictable. As such the combination of Eads et al. and Solinas et al. is maintained. Further, MPEP 2145 [R-6] VIII states

> "The mere age of the references is not persuasive of the unobviousness of the combination of their teachings, absent evidence that, notwithstanding knowledge of the references, the art tried and failed to solve the problem." *In re Wright*, 569 F.2d 1124, 1127, 193 USPQ 332, 335 (CCPA 1977) (100 year old patent was properly relied upon in a rejection based on a combination of references.). See also *Ex parte Meyer*, 6 USPQ2d 1966 (Bd. Pat. App. & Inter. 1988) (length of time between the issuance of prior art patents relied upon (1920 and 1976) was not persuasive of unobviousness).

As such the MPEP is clear that the mere age of the references is not persuasive absent evidence that the art tried and failed to solve a particular problem.

(D) The reply asserts that the instant invention has been licensed to a third party (p. 14 2nd paragraph). The reply asserts that the existing licensing agreement indicates the commercial success of the method as well as its suitability to solve long standing needs within the field of methylation analysis (p. 14 2nd paragraph).

These arguments have been fully reviewed but have not been found persuasive.

The reply seems to be asserting long felt need. The applicant is directed to MPEP 716.04 [R-2] for long felt need. The MPEP states that establishing long felt need requires objective evidence that an art recognized problem existed in the art for a long period of time without solution. The MPEP discloses that it depends on several factors. 1. The need must have been persistent one that was recognized. 2. The long felt need must not have been satisfied by another before the invention. 3. The invention must in fact satisfy the long felt need. The reply has not provided any evidence or arguments that conditions 1-3 are meet. The reply seems to be asserting that the licensing of the invention shows the secondary considerations of long felt need. However MPEP 2144.04 III states that licensing of a patent (or in this case a patent application) is insufficient to show the nexus between the merits of the invention and the licenses and as thus did not establish secondary consideration of commercial success (Iron Grip Barbell Co., Inc. v. USA Sports, Inc., 392 F.3d 1317, 1322, 73 USPQ2d 1225, 1228 (Fed. Cir. 2004).

9. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eads et al. (Nucleic acids Research 2000 Vol. 28 p. e32) in view of Solinas et al. (Nucleic acids Research 2001 Vol. 29 p. e96) as applied to Claims 1-2 and 4-28 and in further view of Berlin et al. (US Patent Application Publication 2006/0183128 August 17, 2006).

The combination of Eads et al. and Solinas et al. teaches a method for detection

of cytosine methylation in DNA, however, Eads et al. and Solinas et al. do not teach the addition of cytosine deaminase.

Berlin et al. teaches a method of DNA methylation. With regard to Claim 3, Berlin et al. teaches cytosine deaminase to use in methylation reaction (paragraph 166 p 17).

Therefore it would have been prime facie obvious to one of ordinary skill in the art to modify the methylation method of Eads et al. and Solinas et al. to include the reaction of cytosine deaminase as taught by Berlin et al. The ordinary artisan would be motivated to modify the methylation method of Eads et al. and Solinas et al. to include a reaction step with cytosine deaminase because Berlin et al. teaches that cytosine deaminase will convert cytosine bases which are unmethylated at the 5' position to uracil to differentiate between methylated and unmethylated cytosine bases (paragraph 166 p. 17). The ordinary artisan would be motivated to treat the DNA with cytosine deaminase such that there is a detectable difference between methylated and unmethylated cytosine bases.

Response to Arguments

The reply asserts that the combination of Eads et al. and Solinas et al. is not obvious in view of using Scorpion primers in a bisulfite treated assay (p. 15 2nd paragraph).

The arguments presented in the reply have been fully reviewed but have not been found persuasive.

As discussed in the rejection of the claims over Eads et al. and Solinas et al. presented above is maintained for the independent claims. As such the rejection of Eads et al, Solinas et al and Berlin et al. for claim 3 is maintained.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1-4, 15-16,18 of copending Application No. 11716207 in view of Solinas et al. (Nucleic acids Research 2001 Vol. 29 p. e96).

Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1,4,5-6 of the instant application is drawn to detecting cytosine methylation in DNA comprising reacting with a chemical or an enzyme, amplifying with a polymerase and at least one primer, separating the extension, and detecting the hybridization. Claim 1-3 and 18 of application no. 11716207 is drawn to the same method steps however, application 11716207 does not claim that the primer is joined with a probe via a linker.

Claims 2-3 of the instant application and Claim 16 of application no. 11716207 are both drawn to bisulfite reagent.

Claim 7 of the instant application and Claim 15 of application no. 11716207 are drawn to quencher fluorescent dye pairs.

Claim 17 of the instant application and Claim 4 of application no. 11716207 are both drawn to simultaneously amplify.

Application 11716207 does not claim that the primer is joined with a probe via a linker.

Solinas et al. teaches using Scorpion primers in PCR assays (abstract). With regard to Claim 1, Solinas et al. teaches a primer whose 5' end is joined with a probe via a linker (e.g. Scorpion primer) (Figure 1).

With regard to Claim 8, Solinas et al. teaches the probe forms a hairpin shape (p. 1 2nd column 1st paragraph).

With regard to Claim 9, Solinas et al. teaches the probe bears two signal components separated in the inactive form and activated after hybridization (Figure 1A).

With regard to Claim 10, Solinas et al. teaches detecting the signal using FRET (p. 3 1st column 1st paragraph).

With regard to Claim 11, Solinas et al. teaches a duplex Scorpion format wherein there is a signal on the probe and a signal on another oligonucleotide (Figure 1B).

With regard to Claim 12, Solinas et al. teaches detecting the signal using FRET (p. 3 1st column 1st paragraph).

With regard to Claim 13, Solinas et al. teaches a duplex Scorpion format wherein there is a signal on the probe and a signal on another oligonucleotide thereby separating the signals in the inactive form (Figure 1B).

With regard to Claim 14, Solinas et al. teaches a method wherein the probe comprises a signal and the other oligonucleotide bears a signal and under hybridization there is a signal (Figure 1b).

With regard to Claim 15, Solinas et al. teaches detecting the signal using FRET (p. 3 1st column 1st paragraph).

With regard to Claim 16 Solinas et al. teaches another binder binds in immediate proximity to the probe (Figure 1B).

With regard to Claim 18, Solinas et al. teaches that two scorpion primers can be used (Table 2).

With regard to Claim 19, Solinas et al. teaches that each Scorpion primer has a different signal (Table 2).

With regard to Claims 20, 21, and 28, Solinas et al. teaches Scorpion primers can be used to detect differences in nucleic acid structure (abstract). It would be obvious to design Scorpion primers to detect methylation and nonmethylated areas of the nucleic acid to use the primers in the methylation assay of Eads et al. Eads et al. teaches designing probes which hybridize to methylated and nonmethylated nucleic acid structures (Figure 1 of Eads et al.).

With regard to Claims 22-24, Solinas et al. teaches a probe with a quencher and a dye molecule which are in the inactive form when in spatial proximity (e.g. hairpin form) and are activated by hybridization of the probe to a primer extension product (Figure 1A).

With regard to Claims 25-27, Solinas et al teaches an assay wherein the probe comprises a dye molecular and another oligonucleotides comprises a quencher and when the two are close they are inactive but after hybridization they are active (e.g. a duplex) (Figure 1B).

Therefore it would have been prime facie obvious to one of ordinary skill in the art to modify the methylation method of application 11716207 to include Scorpion primers linked to probes as taught by Solinas et al. The ordinary artisan would be motivated to modify the methylation method of application 11716207 to include Scorpion primers linked to probes as taught by Solinas et al., because Solinas et al. teaches the use of Scorpion primers in PCR assays allows an intermolecular probe-

target interaction which results in a very fast and reliable detection system (p. 1 2nd column 2nd paragraph). Therefore the ordinary artisan would be motivated to use Scorpion primers to detect methylation and nonmethylation sites fast and reliably.

Accordingly, the claims of application 11716207 and the claims of the instant application are coextensive in scope and not patentably distinct form each other.

This is a provisional obviousness-type double patenting rejection.

Response to arguments

The reply traverses the rejection. A summary of the arguments presented in the reply is summarized below with response to arguments following.

The reply asserts that application '207 does not claim that the primer is joined with a probe via a linker (p. 15 2nd to last paragraph). The reply asserts that claim 1 of '207 application by no means relates to the detection of cytosine methylation in DNA as claimed in the instant application (p. 16 1st paragraph). The reply asserts that based upon arguments of Solinas et al. and Eads et al. presented above that there is no motivation to combine the use of a primer joined with a probe via a linker (p. 16 2nd paragraph).

These arguments have been fully reviewed but have not been found persuasive.

Claim 1 of '207 does relate to detection of cytosine methylation in DNA, Claim 1 is drawn to a method of subjecting a sample to methylation analysis. Further it discloses that this methylation analysis can be in the form of Methyl Light and Scorpion primers (p. 31 2nd paragraph). Further, as presented above, the arguments against the

combination of Eads and Solinas have been fully reviewed but have not been found persuasive based upon the response to arguments presented above.

Conclusion

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE SALMON whose telephone number is (571)272-3316. The examiner can normally be reached on Monday - Friday 9AM-530PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Katherine Salmon

/Sarae Bausch/
Primary Examiner, Art Unit 1634